DIVISION OF INTRAMURAL RESEARCH

NAEHS COUNCIL UPDATE

MAY 2003

DIR Recruitments

Chief, Laboratory of Computational Biology and Risk Analysis
An international search is being conducted for a tenured investigator to serve as Chief of the Laboratory of Computational Biology and Risk Analysis. The candidate will be expected to:

- Develop and maintain a strong personal research effort in the general area of bioinformatics, particularly as it relates to biological networks, proteomics and genomics.
- Provide overall leadership for the existing principle investigators within the LCBRA who study the development of laboratory methods for humans and animals combined with computational, statistical and mathematical methods to further our understanding of the mechanisms underlying environmental disease.
- Recruit talented investigators to the LCBRA and provide a focus for collaborations within the NIEHS.

The Candidate should be a senior investigator with an international reputation in a research area within the broad context of bioinformatics and its relationship to the environment. Possible research areas include but are not limited to mathematics, statistics, genetics, bioengineering and molecular biology. The successful candidate will also have an outstanding publication record and proven history of research leadership. A search committee chaired by Dr. Clarice Weinberg, Chief, Biostatistics Branch is reviewing applications.

Tenure-track Bioinformaticist
The Biostatistics Branch is conducting a nationwide search for a tenure-track investigator with training and experience in bioinformatics. The person selected will focus activities upon developing novel methods related to toxicogenomics, such as developing and evaluating data mining approaches for elucidating characteristic patterns in gene expression array or proteomic data in order to facilitate searches for functionally-coordinated families of genes related to disease processes or response to toxicants. Improved quantitative methods for functional genomics and data mining are needed to make full scientific use of the toxicogenomics data being produced by the NIEHS Microarray Center and the National Center for Toxicogenomics. A search committee chaired by Dr. Douglas Bell, Laboratory of Computational Biology and Risk Analysis has begun interviewing candidates.

Tenure-track Immunologist
The Laboratory of Pulmonary Pathobiology is conducting a national search for a cellular/molecular immunologist. The candidate will be expected to establish a high-quality independent research program in pulmonary immunology in a laboratory with diverse research interests and backgrounds. The successful candidate will have research strengths in, but not necessarily limited to, pulmonary biology (such as mechanisms of tolerance, allergy, adaptive and/or innate immune response to respiratory infections, etc).

A search committee chaired by Dr. John Drake, Chief or the Laboratory of Molecular Genetics is interviewing candidates.

Tenure-track Environmental Epidemiologist
The Epidemiology Branch has conducting a national search for an environmental epidemiologist. This person will be expected to develop an outstanding research program on the effects of environmental exposures and risks of chronic disease. Applicants with demonstrated research interests in biological mechanisms and etiology of (not limited to) neurodegenerative diseases, diabetes, multiple sclerosis, renal disease, cardio-respiratory diseases; and such exposures as pesticides, metals, and/or solvents are most welcome. A search committee chaired by Dr. Steven Kleeberger, Chief of the Laboratory of Pulmonary Pathobiology is interviewing candidates.

Staff Scientist Biostatistician
The Biostatistics Branch is conducting a national search for a statistician to collaborate closely with the National Toxicology Program. The successful candidate will provide statistical leadership and consulting support for the National Toxicology Program and will also develop methods related to design and analysis of toxicology studies. Applicants should have with experience in statistical consulting and a demonstrated ability with problems in applied statistics. A selection has been made, pending approval by NIH.

Tenure-track or tenured Biostatistician--Statistical Genetics
The Biostatistics Branch has conducted an international search for a tenure-track or tenured statistician to conduct independent research on methods development in statistical genetics. The successful candidate will be expected to develop statistical methods for family-based studies aimed at identifying and mapping genes that influence risk modifying quantitative traits or diseases or that interact with the environmental agents that cause human disease. An offer has been extended to a leading candidate.

Staff Scientist--Toxicologic Pathologist
The Laboratory of Experimental Pathology is conducting a national search for a toxicologic pathologist to provide support and peer review for the National Toxicology Program toxicity and carcinogencity studies and to provide support for NIEHS researchers. A search committee chaired by Dr. Rick Hailey, Toxicology Operations Branch, has been formed and review of applications will begin before the end of May.

Staff Scientist—Pathologist/Laboratory Animal Vertinarian
The Laboratory of Experimental Pathology is conducting a national search for a laboratory animal veterinarian to provide management, oversight, production support, genetic monitoring and disease surveillance of laboratory animals for the National Toxicology Program. A search committee chaired by Dr. Joseph Roycroft, Toxicology Operations Branch, has been formed and review of applications will begin before the end of May.

Staff Scientist—Bioethics

The Office of Clinical Research is conducting a national search for a bioethicist to be involved with health policy research on the effectiveness of federal and Institutional Review Board regulations in addressing clinical studies and clinical genetics issues. A search committee chaired by Dr. Stephanie London, Epidemiology Branch, has been formed and the position has been advertised.

DIR Recruits

Dr. Trevor K Archer
Chief, Laboratory of Molecular Carcinogenesis

Dr. Archer directs a research group in Chromatin and Gene Expression. The overall goal of his research over the last 10 years has been to understand the mechanisms by which gene expression is initiated in response to physiological and environmental signals and how those signals are mediated by steroid receptors within the context of chromatin. Dr. Archer and colleagues have pursued two highly interactive objectives. The first is to provide a molecular definition of the relationship between nuclear receptors, chromatin remodeling machines and promoter chromatin structure in the regulation of steroid receptor activity using the mouse mammary tumor virus (MMTV) system as a model for a steroid hormone activated promoter. The wealth of prior information, extensive reagents and resources on this model will allow Dr. Archer to pursue a series of goals that are not possible in other systems. The second objective is the development of additional model systems to understand glucocorticoid, progesterone and estrogen receptors (GR, PR, ER). This objective has resulted in initial characterization of the human cathepsin D and inhibitor of nuclear factor Kappa B alpha genes. The research efforts of the Archer lab are informed by the overwhelming evidence that a full understanding of transcriptional control requires an appreciation for roles played by the chromatin structure of target genes and the molecular machines that are required to unleash the regulatory potential of steroid receptors. The approach has been bi-directional with efforts geared to understanding transacting proteins and the protein architecture of chromatin that is subject to post-translational modifications. Studies have focused on the mammalian chromatin remodeling complex that is the homologue of the yeast SWI/SNF complex and its interactions and regulation by the glucocorticoid and progesterone receptors. The activity of this complex has been evaluated in the context of the chromatin within human and mouse cells. Using the MMTV promoter as the primary model system, Dr. Archer and colleagues have paid particular attention to the phosphorylation of histone H1 and the acetylation of the core histones. The nature of many of the models, human and mouse beast cancer cells, is also indicative of Dr. Archer's active interest in women's health and breast cancer. Additional research in the Archer group examines the epigenetic regulation of the human breast cancer susceptibility gene BRCA1 (initially identified at the NIEHS) and the estrogen receptor regulation of the protease cathepsin D, the over-expression of which, is closely associated with a poor clinical outcome for patients with breast cancer. Dr. Archer has served as chair of the National Cancer Institute of Canada Peer Review Panel on Cell Cycle, Hormone/Steroid Receptors and Signal Transduction, as a member of an NIH Study Section (CDF-6) and as a reviewer for the National Research Foundation of South Africa.

<u>Publications</u>:

Fryer, C.J. and Archer, T.K.: Chromatin remodeling of the glucocorticoid receptor requires the BRG1 complex. Nature 393: 81-91,1998.

Bhattacharjee, R.N., Banks, G.C., Trotter, K.W., Lee, H-L, and Archer, T.K.: Histone H1 phosphorylation by Cdk2 selectively modulates MMTV transcription through chromatin remodelling. Mol. Cell. Biol. 21: 5417-5425, 2001.

Mancini-DiNardo, D.N., Butcher, D.T., Robinson, D.P., Archer T.K., and Rodenhiser, D.I.: Functional analysis of CpG methylation in the BRCA1 promoter region. Oncogene 20: 5331-5340, 2001.

Banks. G.C., Deterding, L.J., Tomer, K.B., and Archer, T.K.: Hormone mediated dephosphorylation of specific histone H1 isoforms. J. Biol. Chem., 276: 36467-36473, 2001.

Deroo, B.J. and Archer, T.K.: Glucocorticoid receptor activation of the IkBa promoter within chromatin. Mol. Biol. Cell. 12: 3365-3374, 2001.

Deroo, B.J., Rentsch, C., Sampath, S., Young, J., DeFranco, D.B. and Archer T.K.: Proteasomal inhibition enhances glucocorticoid receptor transactivation and alters its sub-nuclear trafficking. Mol. Cell Biol., 22: 4113-4123, 2002

Hebbar, P.B. and Archer T.K.: Nuclear factor 1 (NF1) is required for both hormone dependent chromatin remodeling and transcriptional activation of the MMTV promoter. Mol. Cell Biol., 23: 887-898, 2003

Dr. Rachel Neal
Head, Protein Microcharacterization Facility

Dr. Rachel Neal recently joined the Mass Spectrometry Group as the Head of the Protein Microcharacterization Facility. She received a PhD in chemistry on the catastrophic biological effects of high dose radiation from the University of Missouri-Rolla in 1999. Concurrently, she published several papers on the biological effects of low-level Pb-exposure. As a post-doctoral fellow at the National Eye Institute, NIH, she demonstrated that alterations in protein post-translational processing occurred in the lens following low-level oral Pb exposure in rats and induced opacities in lens organ culture following modifications in cytoskeletal and crystallin proteins. She also created a topographical map of proteins expressed in the human vitreous humor.

The Microcharaterization Facility is currently involved in multiple collaborations involving identification of protein-protein interaction sites and mapping of post-translational protein modification sites. In addition, the facility provides DIR scientists with cutting-edge mass spec services for the identification of proteins from gels and solutions.

Publications:

Neal, R., Matthews, R.H., Lutz, P., and Ercal, N.: Antioxidant role of N-acetyl cysteine isomers following high dose irradiation. Free Radic. Biol. Med., 34: 689-95, 2003.

Neal, R, Zigler, J.S., Jr., and Bettelheim, F.A.: On the equilibrium between monomeric alpha-lactalbumin and the chaperoning complex of alpha-crystallin. Biochem. Biophys. Res. Commun., 280: 14-18, 2001.

Neal, R., Cooper, K., Kellogg, G., Gurer, H., and Ercal, N.: Effects of some sulfur-containing antioxidants on lead-exposed lenses. Free Radic. Biol. Med. 26: 239-243, 1999.

Neal, R., Cooper, K., Gurer, H. and Ercal, N. Effects of N-acetylcysteine and 2,3-dimercaptosuccinic acid on lead induced oxidative stress in rat lenses. Toxicology 130: 167-174, 1998.

Dr. Robert Petrovich
Head Protein Expression Core Facility

Dr. Robert Petrovich has recently joined the NIEHS as Head of the Protein Expression Core Facility. He received his Ph.D. in biochemistry from the University of Wisconsin-Madison in 1992. His thesis research focused on identifying the metal cofactors for lysine-2,3-aminomutase, and determining their role in the mechanism of the enzyme. Dr. Petrovich then moved on to a post-doctoral research position in the Chemistry Department at the University of Wisconsin-Madison where he studied the method for the activation of soluble guanylyl cyclase by nitric oxide. Dr. Petrovich then moved to the laboratory of Dr. Eileen Jaffe at the Fox Chase Cancer Center, where he studied the mechanism of porphobilinogen synthase. In 1999, Dr Petrovich was hired by Novartis/Syngenta to develop high throughput screens for the discovery of new agro-chemicals. In the course of this work he directed the Syngenta effort to establish a rapid parallel method for the expression of protein targets. The output of this effort was 100 new soluble proteins per year from genetically validated targets.

Dr. Petrovich's current role in the Laboratory of Structural Biology is to establish a protein expression core facility. Current ongoing projects include setting up a method to rapidly determine the best method to express a protein from a gene. This effort includes *E. coli*, baculovirus/insect cell and mammalian cell expression systems. Dr. Petrovich also plans to pursue the implementation of general refolding techniques to produce soluble proteins.

Publications:

Petrovich, R.M. and Jaffe, E.K.: Magnetic resonance studies on the active site and metal centers of Bradyrhizobium japonicum porphobilinogen synthase. Biochemistry 36: 13421-13427, 1997.

Petrovich, R.M., Litwin, S., and Jaffe, E.K.: Bradyrhizobium japonicum porphobilinogen synthase uses two Mg(II) and monovalent cations. J. Biol. Chem. 271: 8692-8699, 1996.

Petroivch, R.M., Ruzicka, F.J., Reed, G.H., and Frey, P.A.: Characterization of iron-sulfur clusters in lysine 2,3-aminomutase by electron paramagnetic resonance spectroscopy. Biochemistry 31: 10774-10781, 1992.

Petroivch, R.M., Ruzicka, F.J., Reed, G.H., and Frey, P.A.: Metal cofactors of lysine-2,3-aminomutase. J. Biol. Chem. 266: 7656-7660, 1991.

TRAINING AND MENTORING

2003 NIEHS/NTA Science and Career Fair

The Sixth Annual NIEHS/NTA Biomedical Science and Career Fair was held on April 25, 2003 in the Rodbell Conference Center, NIEHS. The keynote speaker was Dr. Yvonne T. Maddox, Deputy Director, National Institute of Child Health and Human Development, NIH, DHHS. The panel discussion this year focused on "Career Opportunities in Science." It was moderated by Dr. Thomas Kunkel, Chief, Laboratory of Structural Biology, and Scientific Program Director, Environmental Biology Program, NIEHS. Panel participants included Dr. Maddox; Dr. Mohammed Bourdi, Staff Scientist, Laboratory of Molecular Immunology, NHLBI, NIH; Dr. Allison Chausner, Health Scientist Administrator, Division of Neuroscience and Behavioral Research, Translation Research Branch, NIDA, NIH; Dr. Adnan Hammad, Director, Community Health and Research Center, Detroit, MI; Dr. J. Eric McDuffie, Senior Scientist, Toxicologic Pathology, Pfizer Global Research and Development, Ann Arbor, MI; Dr. Viviana Simon, Program Manager, Society for Women's Health Research, Washington, D.C.; and Dr. Abdelkrim Smine, Senior Research Scientist, Global Assistance Initiative, United States Pharmacopeia, Rockville, MD. Other events at the Science and Career Fair included a poster session with 62 posters and a Career Fair with 17 participating companies.

There were more than 270 registered attendees from universities and research institutions in the Triangle Area and the rest of North Carolina. The NIEHS, CIIT Centers for Health Research, the Burroughs Wellcome Fund, S & M Separation Technologies, Inc., Taylor and Francis, Merck and Co., and Sigma Xi, cosponsored this event.

International Activities in the DIR 2002

Dr. Kamel Abdo (Toxicology Operations Branch) has a collaborative study with scientists at the Department of Community, Environmental, and Occupational Medicine, Faculty of Medicine, Ain Shams University, Cairo, Egypt to investigate the association between pesticide use in Egypt and occurrence of different cancers among Egyptians and a collaboration with scientists at the Center for Environmental and Occupational Health Sciences, Birzeit University, Ramallah, Palestine to determine indices of nutritional status of children.

Dr. Steven Akiyama (Laboratory of Molecular Carcinogenesis and Deputy Scientific Director) served on a Grant Review Committee for the Italian Ministry for Education University and Research and as an external grant reviewer for the Michael Smith Foundation for Health Research, Vancouver, BC, Canada.

Dr. Trevor Archer (Chief, Laboratory of Molecular Carcinogenesis) has collaborative research projects with scientists at the Child Health Research Institute, University of Western Ontario, London, Ontario, Canada to perform a functional analysis of CpG methylation in the BRCA1 promoter region.

Dr. David Armstrong (Acting Chief, Laboratory of Environmental Neuroscience) has a collaboration with scientists in the Department of Physiology at the University of Edinburgh to study the structural basis for potassium channel regulation by the cAMP-dependent protein kinase and is serving on a Grant Review Committee for the Italian Ministry for Education University and Research for the topics of calcium signaling and signal transduction.

Dr. Donna Baird (Epidemiology Branch) is working with Drs. Clare Weinberg (Biostatistics Branch), Allen Wilcox (Epidemiology Branch), and Donna Baird (Epidemiology Branch) in collaboration with researchers at the Department of Epidemiology and Social Medicine, University of Arhus, Denmark, to study pre-eclampsia and infertility through the Danish National Birth Cohort, an ongoing prospective study of pregnancies in Denmark.

Dr. Perry Blackshear (Director, Office of Clinical Research and Laboratory of Signal Transduction) has collaborations with scientists at McGill University, Montreal, Canada to study genetic modifiers of insulin action with PHAS-I knockout mice (which were developed at the NIEHS); with scientists at the Institute of Immunology, Biomedical Sciences Research Center 'Alexander Fleming', Vari, Greece to study interactions between TTP knockout mice and TNF and TNF receptor knockout and knock-in mouse lines; with scientists at the Institute of Clinical Biochemistry and Pathobiochemistry, Medical University Clinic, Würzburg, Germany to study P38 kinase – TTP interactions using TTP knockout mice (which were developed at the NIEHS); with scientists at the University of Manchester, UK to resequence the promoter and exons of the ZFP36 gene, encoding TTP, in University of Manchester population of patients with well-characterized forms of juvenile rheumatoid arthritis; at the University of Udine, Italy to

resequence the promoter and exons of the ZFP36 from patients with rheumatoid arthritis who either responded or didn't respond to anti-TNF therapy; with scientists at the University of Zurich, Switzerland to study interstitial cell MARCKS and MLP expression in the normal kidney and in kidneys of mice with fibroproliferative diseases; with scientists in the Department of Applied Biochemistry and Biology, Faculty of Agronomy, Gembloux, Belgium to study interactions between bovine leukemia virus, HTLV, and TTP in the pathogenesis of bovine leukemia; with scientists in the Division for Immunology, Zurich University, Switzerland to evaluate TTP and TNF mRNA kinetics and responses in farm children exposed to low or high endotoxin levels; with scientists in the Department of Molecular Genetics, The Weizmann Institute of Science, Rehovot, Israel to work on MARCKS and MLP in animal models of lissencephaly syndromes; with scientists in the Department of Veterinary Microbiology, University of Saskatachewan, Saskatoon, Canada to work on *Trypanosoma congolense* infections in TTP deficient mice; with scientists at the University of British Columbia, Canada to evaluate telomere length in mice deficient in a RECQL helicase, which may have a cancer-susceptible phenotype; with scientists at the Zentrum für Molekulare Neurobiologie, Universität Hamburg, Germany to study MARCKS interacting proteins and peripheral nerve migration; and with scientists in the Department of Pathology, Yonsei University, College of Medicine, Seoul, Korea to work on mononucleotide repeats in MARCKS sequences in colon cancer. Dr. Blackshear also has a Cooperative Research and Development Agreement with Oxford Glycosciences, Abingdon, UK to look at proteomics modifications in diabetes as indicators of disease status and status of complications.

Dr. Rajendra Chhabra (Toxicology Operations Branch) was invited by the International Program on Chemical Safety to participate in, and serve as a WHO Temporary Adviser to, the Tenth Final Review Board Meeting for Concise International Chemical Assessment Documents held in Monks Wood, UK, September, 2002 to review and finalize draft Concise International Chemical Assessment documents (CICADs), which are intended to provide an assessment of the health and environment hazards and risks of chemicals, together with advice on prevention of exposure and protective measures. The draft CICADs finalized in this meeting were arsine, 1,1-dichloroethane, ethylene oxide, hydrogen sulphide and sulphides, thiourea, and trichloropropane.

Theodora Devereux (Laboratory of Molecular Carcinogenesis) hosted the sabbitical of a scientist from Queens University, Kingston, Ontario, Canada in her lab to collaborate on a study to examine global expression changes in sets of mouse lung tumor cell lines with different invasiveness based on movement through Matrigel.

Dr. John Drake (Chief, Laboratory of Molecular Genetics) is serving as the DHHS mentor and a collaborator with scientists in Tbilisi, Georgia at the G. Eliava Institute of Bacteriophages, Microbiology and Virology. This is a Biotechnology Engagement Program (BTEP) project entitled "Study of Phage-Specific "Killer" Proteins" to understand just how bacteriophages used as antibiotics kill at the molecular level. He also has a collaborative research program with scientists at the Institute of Biochemistry and Biophysics, Polish Academy of Sciences, Warsaw investigating the structural basis

of DNA polymerse fidelity and serves on the Executive Board of the International Genetics Federation, an umbrella organization of numerous national genetics societies.

Dr. E. Mitch Eddy (Laboratory of Reproductive and Developmental Toxicology) served as an external examiner for grant applications to the Michael Smith Foundation for Health Research, Vancouver, BC, Canada; the Wellcome Trust, London, England; Comitato Telethon Fondazione ONLUS, Rome, Italy; and the National Health and Medical Research Council, Australia and is serving as the NIH mentor for an MD-PhD student in the Tel Aviv University – NIH Program for Israeli Predoctoral Biomedical Researchers on a project is to isolate cDNAs for the ubiquitously expressed calpain 1 and calpain 2 and the spermatogenic cell-specific calpain 11. Dr. Eddy has collaborations with researchers at the Department of Anatomy and Reproductive Cell Biology, Miyazaki Medical College, Miyazaki, Japan to clone cDNAs for proteins involved in fertilization; with scientists in the Department of Life Sciences, Kwangju Institute of Science and Technology (K-JIST), Kwangju, Korea to produce a conditional mutant for protamine 2; with scientists in the Department of Bioenvironmental Medicine, Graduate School of Medicine, Chiba University, Chiba, Japan to target sequences for the spermatogenic cell-specific form of type 1 hexokinase; with scientists in the Department of Embryology, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel to express and localize calpain-1, -2, and –11 in spermatogenic cells; with scientists at the Instituto de Biologia y Medicina Experimental, Buenos Aires, Argentina to produce a targeted mutation of the gene encoding epididymal protein DE; with scientists at the Monash Institute of Reproduction and Development, Monash University, Clayton, Victoria, Australia to study genetics of human male infertility; with scientists in the Laboratory of Experimental Animals, Department of Molecular Biology and Immunology, National Institute of Agrobiological Sciences, Tsukuba, Japan to study regulation of expression of genes essential for male fertility.

Dr. John French (Laboratory of Molecular Toxicology) organized and participated the International Union of Toxicology workshops in Nanjing, China in October 2001 and organized and participated in the International Workshop on Genetic Toxicology in Plymouth England in June 2002.

Dr. Dori Germolec (Laboratory of Molecular Toxicology) is currently serving on the World Health Organization International Program on Chemical Safety (IPCS) Task Group to compose the Environmental Health Criteria "Scientific Principles and Methods for Assessing Autoimmunity Associated with Exposure to Chemicals;" and on the organizing committee for the US/Japan joint meeting entitled "Arsenic in Biology and Medicine," the purpose of which was to discuss the dose-response relationship for cancer and non-cancer endpoints for target organs of arsenic toxicity and to determine the relevance of low-level effects relating to these endpoints in light of increased worldwide exposures. Dr. Germolec is part of a collaboration organized by the International Life Sciences Institute to evaluate the utility of the modified local lymph node assay as a means of determining the potential for drugs to cause life-threatening hypersensitivity reactions.

Dr. Beth Gladen (Biostatistics Branch) has collaborations with investigators at the Institute of Pediatrics, Obstetrics, and Gynecology, Kyiv, Ukraine; the National Medical University, Kyiv, Ukraine; Kyiv Medical Academy of Post-Diploma Education, Kyiv, Ukraine, and the University of Bristol, Bristol, UK to examine pollution and reproductive outcomes in two cities in Ukraine; with scientists at Health Canada, Ottawa, Canada to examine patterns of exposure to different polychlorinated biphenyl congeners in milk samples collected from women across Canada in 1992 in order to determine whether health effects of different congeners could be examined separately; with scientists at the University of Southern Denmark, Odense, Denmark; DK-Teknik Energy and Environment, Søborg, Denmark; Erasmus University, Rotterdam, The Netherlands; University Hospital, Groningen, The Netherlands; Heinrich-Heine-University, Düsseldorf, Germany; Institute of Environmental Toxicology, Kiel, Germany; and Laval University, Beauport, Canada on studies of neurodevelopmental effects of transplacental exposure to polychlorinated biphenyls have used different techniques to assess exposure; and with scientists at the Instituto Nacional de Salud Pública, Cuernavaca, México to study effects of the antiandrogen DDE on anthropometric measures at birth.

Dr. Joyce Goldstein (Laboratory of Pharmacology and Chemistry) has a collaboration with scientists from the Department of Pharmacology, Faculty of Medicine, Khon Kaen University, Thailand on an analysis of CYP2C19 polymorphisms in Thai populations.

Dr. Traci M.T. Hall (Laboratory of Structural Biology) has a collaboration with scientists at the Agricultural Biotechnology Center, Plant Biology Institute in Gödöllõ, Hungary to determine the three-dimensional structures of plant viral proteins that suppress post-transcriptional gene silencing.

Dr. Ronald Herbert (Laboratory of Experimental Pathology) attended the World Health Organization/International Agency for Research on Cancer (IARC) Monograph Committee and Chaired the Carcinogenesis Working Group, IARC Working Group Meeting to prepare Volume 82 of IARC Monographs Series on Some Traditional Herbal Medicines, Some Mycotoxins, Naphthalene and Styrene, Lyon France, in February, 2002.

Dr. William Jameson (National Toxicology Program) was the National Toxicology Program representative at the International Agency for Research on Cancer (IARC) Working Group meeting in Lyon, France in February to review the cancer data for some traditional herbal medicines, some mycotoxins, naphthalene and styrene. The reviews and evaluations of this Working Group resulted in the publication of the IARC Monograph on the Evaluation of Carcinogenic Risks to Humans, Vol. 82, Some Traditional Herbal Medicines, some Mycotoxins, Naphthalene and Styrene.

Dr. Anton Jetten (Laboratory of Pulmonary Pathobiology) had collaborations with scientists from the Department of Molecular Medicine, University of Osaka, Osaka, Japan to study the function of the nuclear orphan receptor RORgamma; with scientists at the Department of Mucosal Immunology, University of Tokyo, Tokyo, Japan to study the role of the nuclear orphan receptor in the immune system; with scientists at the Department of Molecular Cell Biology, Weizmann Institute of Science, Rehovot, Israel to

study the function of p63 in the differentiation of esphageal and tracheal epithelium; and with scientists at the Department of Structural Biology and Structural Genomics, Institut de Génétique et de Biologie Moléculaire et Cellulaire, Illkirch, France to study the structure of the RORgamma protein.

Dr. Steven Kleeberger (Chief, Laboratory of Pulmonary Pathobiology) has a collaboration with researchers at the National Institute of Health and Medical Research, INSERM, Paris to investigate the genetic basis for susceptibility to the effects of coal dust in miners.

Dr. Thomas Kunkel (Chief, Laboratory of Structural Biology) was an organizer of the Symposium on "Structural Biology of Replication and Its Relevance to Mutation Research" at the Eighth International Conference on Environmental Mutagens, Shizouka, Japan, October, 2001; and has collaborations with researchers at the Institute for Molecular and Cellular Biology,Osaka University, Japan to study the efficiency and fidelity of DNA synthesis by human DNA polymerase eta; and with scientists at Centro de Biología Molecular Severo Ochoa (CSIC-UAM) Universidad Autónoma, Madrid, Spain to study the biochemical properties and function of human DNA polymerase lambda.

Dr. Larry Lazarus (Laboratory of Computational Biology and Risk Analysis) has collaborations with researchers at the Department of Pharmaceutical Sciences and Biotechnology Center, University of Ferrara, Ferrara, Italy, the Department of Toxicology, University of Cagliari, Cagliari, Italy, and the Department of Human Physiology "Vitorio Erspamer," Unviversity La Sapienza, Rome, Italy to develope highly specific antagonists and agonists for the δ- and μ-opioid receptors, or bifunctional compounds for both receptors; and with researchers on the Faculty of Pharmaceutical Sciences and High Technology Research Center, Kobe Gakuin University, Kobe, Japan; and the Tohoku Pharmaceutical University, Sendai, Japan to develope unique analogues for the μ-opioid receptor based on simple structural motifs.

Dr. Stephanie London (Epidemiology Branch) has collaborations with scientists at the National Institute of Public Health, Cuernavaca, Mexico to study the genetics of childhood asthma in Mexico City; with investigators at the National University in Singapore and the University of Southern California to investigate the relation between diet and the incidence of asthma and chronic bronchitis in a cohort of 63,000 adult Singaporeans of Chinese ethnicity; and with scientists at the Wuhan Public Health and Anti-Epidemic Station and the University of Southern California to study indoor air pollutants in relation to childhood respiratory symptoms.

Dr. Matthew Longnecker (Epidemiology Branch) has collaborations with scientists at the Institute of Public Health, University of Southern Denmark, Odense, Denmark; the Department of Pediatrics, Division of Neonatology, Erasmus University and University Hospital/Sophia Children's Hospital, Rotterdam, The Netherlands; the Department of Social and Preventive Medicine, Laval University and Public Health Research Unit, CHUQ Research Center (CHUL), Beauport, Quebec, Canada; the Medical Institute of

Environmental Hygiene at Heinrich-Heine-University Duesseldorf, Duesseldorf, Germany; the Perinatal Nutrition and Development Unit, Department of Obstetrics/Pediatrics, University Hospital Groningen, Groningen, The Netherlands; the Institute of Environmental Toxicology, Kiel, Germany; and DK-TEKNIK Energy & Environment, Soeborg, Denmark to study the comparison of polychlorinated biphenyl (PCB) levels across studies of human neurodevelopment; and with researchers at the National Institute of Public Health in Cuernavaca, Mexico to examine the relation between maternal serum levels of the androgenic DDT metabolite DDE in relation to anthropometric measures in 200 male newborns in Tapachula, Mexico, where there has been recent, high-level exposure to DDT.

Dr. James Mason (Laboratory of Molecular Genetics) has collaborations with scientists at the Institute of Science History and Technology, Russian Academy of Sciences, St. Petersburg, Russia, to characterize telomere-telomere interactions in *Drosophila*; with scientists at the University of Rome, Italy, to characterize a mutation in *Drosophila* that causes telomeric repeat arrays to grow to great lengths; and with scientists at the Institute of Gene Biology, Russian Academy of Sciences, Moscow, Russia, to identify and clone a second mutation that increases telomere length in *Drosophila*.

Dr. B. Alex Merrick (National Center for Toxicogeniomics) was an invited to the Human Proteome Organization (HUPO) Liver Proteome Conference in Beijing, China, October 22-24, 2002.

Dr. David Miller (Laboratory of Pharmacology and Chemistry) has collaborations with scientists at the Department of Pharmacology & Toxicology, Nijmegen Center for Molecular Life Sciences, Nijmegen, The Netherlands to characterize the regulation of xenobiotic export pumps in renal proximal tubule; and with scientists at the Institute for Pharmacy and Biotechnology, University of Heidelberg, Heidelberg, Germany to characterize the role of drug export pumps in blood-brain barrier function. Dr. Miller also hosted a scientist from the National Institute of Toxicological Research, Seoul, Korea in his laboratory and provided training in the conduct of assays of renal cell function (transport in renal slices, measurement of slice respiration, confocal imaging of single renal tubules) that can be used to assess effects of nephrotoxicants.

Dr. Fred Miller (Office of Clinical Research) co-chaired with Dr. Lisa Rider (Office of Clinical Research) the International Workshop on Myositis Outcome Measures and Clinical Trial Design Issues. Dr. Miller is also a member of The International Myositis Collaborative Study Group with scientists from Montreal, Canada; Santiago, Chile; Guatemala City, Guatemala; Mexico City, Mexico; Guadalajara, Mexico; Aachen, Germany; Nijmegen, The Netherlands; Warsaw, Poland; Glasgow, Scotland; Barcelona, Spain; Stockholm, Sweden; New Delhi, India; Tokyo, Japan; and Seoul, South Korea which has been organized to collect standardized data and specimens on myositis patients.

Dr. Yuji Mishina (Laboratory of Reporductive and Developmental Toxicology) has a collaboration with scientists at the Brain Science Institute, RIKEN, Saitama, Japan

Group to uncover the function of bone morphogenic protein signaling in brain development.

Dr. Elizabeth Murphy (Laboratory of Signal Transduction) is serving as a member of the International Council of the International Society for Heart Research.

Dr. Masahiko Negishi (Laboratory of Reproductive and Developmental Toxicology) is a member of the International Advisory committee on the 14th International Symposium on Microsomes and Drug Oxidation and has a collaboration with scientists at Kobe Pharmaceutical University, Japan to perform an X-ray crystallographic analysis of glycosyltransferases involved in heparan sulfate synthesis.

Retha Newbold (Laboratory of Molecular Toxicology) worked with DES Action International providing scientific information on DES exposure and animal models and with the World Wildlife Fund reviewing proposals and providing scientific information on endocrine disrupting chemicals. Ms. Newbold also has collaborations with scientists at the University of Rome "La Sapienza," Italy to study effects of environmental estrogens on development of bone tissue; with scientists at the University of Karlsruhe, Germany to study effects of genistein and daidzein on the developing reproductive tract; with scientists at the University Hospital of Copenhagen, Denmark to study effects of genistein on the developing ovary; with scientists at Bar-ilan University, Ramat-Gan, Israel to test a natural antioxidant found in spinach for hormonal activity; and with scientists at the Okazaki National Research Institute, Japan to study effects of endocrine disrupting chemicals on the developing reproductive tract using fetal or neonatal mouse models.

Dr. Christopher Portier (Chief, Laboratory of Computational Biology and Risk Analysis) participated as a plenary speaker and session chair at the conference on "Light, Endocrine Systems and Cancer" on May 2-3, 2002 in Cologne, Germany sponsored by the German Research Council (DFG); participated in a workshop on "Hepatic preneoplasia: quantitative evaluation in carcinogenesis biossays and relevance for human hepatocarcinogenesis" on June 29-30, 2002 in Heidelberg, Germany; served as the chair of the Science Advisory Board for one aspect of the Finnish Academy of Sciences, Centers of Excellence Program; was asked by the German Cancer Research Insitute (DKFZ) to review research directions on the use of the rat liver focus bioassay by the DKFZ; and represented the Department of Health and Human Services at the Global Mercury Assessment Working Group in Geneva, Switzerland, at the request of the Office of Science Policy within the Office of the Secretary, DHHS, to outline options for consideration at the twenty-second session of the Governing Council/Global Ministerial Environment Forum of the United Nations Environment Program addressing any significant global adverse impacts of mercury, inter alia, by reducing and or eliminating the use, emissions, discharges and losses of mercury and its compounds; improving international cooperation; and ways to enhance risk communication. Dr. Portier also has a collaboration with researchers at the University of Bern, Switzerland on the analysis of data pertaining to receptor-mediated activation of a number of different cellular constructs.

Dr. Michael Resnick (Laboratory of Molecular Genetics) has collaborations with researchers at the National Institute for Cancer Research in Genoa, Italy to study partial-function p53 mutations; with researchers in the Unit of Molecular Carcinogenesis, International Agency for Research on Cancer (WHO), Lyon, France to analyze partial function mutations of p53 and develope a p53 database that includes functional alterations and clinical features; with researchers in the Molecular Immunology Unit, Institute of Child Health, University College London, England to develop an inducible enzyme system in mammalian cells that provides for the production of a single, unique double-strand break in cells of humans; with researchers at the Institute of Veterinary Biochemistry and Molecular Biology, University of Zürich-Irchel, Switzerland to conduct an extensive structure-function investigation of human FEN1 nuclease; and with researchers in Chromosome Replication Group, Laboratories for Biomolecular Networks, Graduate School of Frontier Biosciences, Osaka University, Japan to study a mutation in yeast DNA polymerase epsilon that results in hypermutation and characterize effects of hypermutation on the proofreading (error-correction) function of this protein. Dr. Resnick has also organized an international meeting "Functional consequences of TP53 mutations" to be held at IARC, in Lyon, France, from June 30 to July3, 2003 to explore the importance of various p53 functional mutations and their relevance to cancer as well as to develop further the existing p53 database as IARC.

Dr. John Roberts (Laboratory of Molecular Carcinogenesis) has a collaboration with scientists at the Institute of Cell Biology and Immunology, University of Stuttgart, Germany to work on PKC-mu and its role in tumor cell adhesion to the extracellular matrix.

Dr. Walter Rogan (Epidemiology Branch) was an organizer and host of a multinational meeting in Hanoi to study people affected by Agent Orange, a defoliant used by US troops during the Vietnam War and help to edit the proceedings of the meeting. Dr. Rogan continued 18 years of work in collaboration with scientists at the National Cheng Kung University Hospital in Taiwan to follow children transplacentally exposed to high levels of heat-degraded PCBs.

Dr. Dale Sandler (Acting Chief, Epidemiology Branch) has a collaboration with researchers at the Prague Institute of Advanced Studies, Prague, Czech Republic and the Center for Epidemiological Studies, Pribram, Czech Republic to study cancer risk among underground uranium miners in the Czech Republic.

Dr. Roel M. Schaaper (Laboratory of Molecular Genetics) has collaborations with scientists at the Institute of Biochemistry and Biophysics, Polish Academy of Sciences, Warsaw, Poland to study mechanisms of DNA replication fidelity; and with scientists in the Department of Genetics, St. Petersburg State University, St. Petersburg, Russia to study base analog detoxification by molybdenum-dependent activities, research that is supported by a Collaborative Linkage Grant awarded by NATO.

Dr. James Selkirk (National Center for Toxicogenomics) organized and hosted the US - Japan Panel on Environmental Genomics and Carcinogenesis. This meeting centered around the use of expression array technologies for genes, and new developments in proteomics and emphasized mutual areas of public health interest to both countries and serves as a venue to exchange ideas and collaborative research.

Dr. Steven Shears (Laboratory of Signal Transduction) has collaborations with researchers in the Department of Chemistry, Pohang University of Science and Technology, Korea to characterize a novel, physiologically-relevant reversible kinase/phosphatase with the goal of developing new therapy for both enhancing and promoting mucous secretion (for the common cold, bronchitis and cystic fibrosis); with researchers in the Department of Physiological Sciences, Lund University, Sweden to study the regulation of insulin secretion by inositol phosphates and the relevance to the etiology of type II diabetes; and with researchers at the Institut de Recherches Microbiologiques Jean-Marie Wiame, Université Libre de Bruxelles, Belgium to study yeast as a model for understanding the participation of inositol phosphates in cell responses to environmental stress.

Dr. William Stokes, (National Toxicology Program and Director, NTP Interagency Center for the Evaluation of Alternative Toxicological Methods) participated in a European Centre for the Validation of Alternative Methods scientific symposium on the status of alternative methods convened to recognize ECVAM's tenth anniversary in June 2002 and presented an overview of current and proposed collaborations between NICEATM, the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM), and ECVAM; and NICEATM and ICCVAM, in partnership with the International Life Sciences Institute (ILSI), served on the organizing committee for an international training workshop on *in vitro* and *in vivo* alternative acute toxicity testing methods, which met on February 19-21, 2002, to provide practical information and case studies to facilitate understanding and the implementation of *in vivo* and *in vitro* alternative methods for acute toxicity.

Dr. Kenneth Tomer (Laboratory of Structural Biology) served as an expert in separations for the EU 5th Microproteomics Consortium meeting, July, 2002 in Konstanz, Germany, coordinating development of microfluidic/mass spectrometry approaches to proteomics.

Dr. Clarice Weinberg (Chief, Biostatistics Branch) serves on the Science Council that oversees the work of the Radiation Effects Research Foundation in Hiroshima, Japan to carry out basic and epidemiologic research related to health effects of ionizing radiation; is involved in a collaboration with a reproductive genetic epidemiologist at McGill University, Montreal, Canada, who is studying genetic effects on intra-uterine growth retardation, on gestational survival, and on childhood cancers; and is a co-investigator of a multinational research project on a birth defect, oral clefting (cleft lip and cleft palate) with scientists in Norway.

Dr. Samuel H. Wilson (Laboratory of Structural Biology and Deputy Director) was the founding organizer and a co-chair of the 1st Japan-U.S. DNA Repair Meeting and chaired

the session on base excision repair. He also made a presentation on "Protection against genomic damage by base excision repair and DNA polymerase beta" at the 32nd Annual Meeting of European Environmental Mutagen Society, "DNA Damage and Repair Fundamental Aspects and Contribution to Human Disorders" in Warsaw, Poland.

Dr. Jerrel Yakel (Laboratory of Signal Transduction) has collaborations to study co-assembly of nicotinic acetylcholine receptor $\alpha 7$ and $\beta 2$ subunits to form functional heteromeric nicotinic receptor channels with researchers from the Department of Pharmacology, University College London, England; and with researchers form the Johannes A. van Hooft, University of Amsterdam, Swammerdam Institute for Life Sciences, Amsterdam, the Netherlands to characterize the function and structure of serotonin 5-HT_3 receptors in rat CA1 hippocampal interneurons.

Dr. Darryl Zeldin (Laboratory of Pulmonary Pathobiology) had a collaboration with scientists at the University of Bochum and St. Josef Hospital, Bochum, Germany to study variants in the human *CYP2J2* gene and with scientists at the Tongji Medical Center, Tongji, Peoples Republic of China to study the regulation of endothelial nitric oxide synthase (eNOS) by endothelium-derived hyperpolarizing factors (EDHF) and the relevant signaling pathways involved.

The NIEHS had two projects as part of the Congressionally mandated Agent Orange initiative in Vietnam. The first project, a workshop on the health and environmental effects of Agent Orange/Dioxin in Vietnam was held in March in Hanoi. The second project is ongoing and is focused on the validation of cell-based assays for measuring dioxin levels in soils.

The NIEHS and the National Toxicology Program (NTP) have signed a Memorandum of Understanding (MOU) with the Ramazinni Foundation. The Ramazinni Foundation supports a toxicology program in Bologna which conducts large carcinogenesis bioassays similar to those conducted by the NTP. This MOU sets up a coordinating body between the two agencies to avoid duplication of effort and to provide computing and statistical support to the Ramazinni Foundation by the NTP.

The Korean Government just initiated a new National Toxicology Program. The NIEHS and the US NTP began the development of joint programs with the Korean NTP.

The NTP is collaborating with the World Health Organization to coordinate and summarize research on radiofrequency electric and magnetic fields. This collaboration is aimed at reducing duplication of effort and identifying data gaps in the research on cellular phones that might be met by the NTP.

NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) initiated a joint collaborative validation study in July 2002 with the European Centre for the Validation of Alternative Methods (ECVAM) on *in vitro* methods for assessing acute systemic toxicity. Two U.S. labs and one European lab are conducting the studies, which will evaluate the usefulness of cytotoxicity data for

estimating the acute systemic toxicity potential of chemicals. Preliminary data indicate that *in vitro* cytotoxicity data will reduce the number of animals required and reduce the number of deaths that occur from acute toxicity studies.

NICEATM and the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) organized an international expert panel meeting to assess the validation status of *in vitro* assays proposed for use in the EPA's Endocrine Disruptor Screening Program (EDSP) on May 21-22, 2002, which involved scientists from the UK, Canada, Japan, and Denmark, to review estrogen receptor (ER) and androgen receptor (AR) binding and transcriptional activation (TA) assays, provide recommendations on test methods and technologies that should be given priority for further development and validation, and recommend substances that should be used for validation studies, and minimum procedural standards that should be incorporated in the various assays.

National Toxicology Program (NTP)
Update May 2003

New Database Available

The NTP is creating a new database to allow searches of its study data using the web. Currently the NTP is developing programming tools for accessing the data, and is interested in obtaining feedback from the public on its use of these new searches.

To access the database and do a search go to the NTP homepage (http://ntp-server.niehs.nih.gov) and select "NTP Study Information." On this page are new options for accessing the database and doing a search. (Hyperlinks on this page are shown here in italics.) Go to:

SEARCH THE NTP STUDIES DATABASE

- *Available Data on Individual Studies*
- Pathology
  - *Incidence rates* for completed chronic and prechronic studies collected in the Toxicology Database Management System (TDMS)
  - *Individual animal* pathology data for completed chronic studies collected in the NTP's Toxicology Database Management System (TDMS) and Carcinogenesis Bioassay Data System (CBDS)

The first search category "Available Data on Individual Studies" allows the user to enter a chemical name or CAS # and retrieve information about the types of studies (*e.g.*, chronic exposure studies, reproductive/development, genetic toxicity, etc.) that are completed and to determine which studies have data available in electronic format. The types of data that might be available are clinical chemistry, hematology, organ weights, body weights, survival, clinical observations and pathology.

The second category, "Pathology" includes two links to search through the NTP pathology databases. Under this heading the first link retrieves the incidence rates and the second link retrieves individual animal evaluations.

The NTP welcomes receiving input from persons who try the database. Please send your queries, comments, and suggestions to: ntpwm@niehs.nih.gov

NTP Board of Scientific Counselors

The next meeting of the NTP Board of Scientific Counselors Technical Reports Review Subcommittee is scheduled for May 22, 2003 at the NIEHS. This subcommittee of the NTP Board of Scientific Counselors meets regularly to review the findings and conclusions of NTP toxicology and carcinogenesis studies.

The primary agenda topic is the peer review of six draft Technical Reports (TR) of rodent toxicology and carcinogenesis studies conducted by the NTP. At this meeting the NTP will unveil a new technical report series for studies using genetically modified models. The first two reports in this series are on aspartame and acesulfame potassium.

Chemical (Primary Uses)	**Report #**
Propylene glycol mono-*t*-butyl ether (Solvent)	TR 515
2-Methylimidazole (Chemical and pharmaceutical intermediate)	TR 516
Triethanolamine (Industrial and manufacturing applications)	TR 518
Stoddard solvent IIC (Paint and dry cleaning solvent)	TR 519
Aspartame (Artificial sweetener)	GMM 1
Acesulfame potassium (Artificial sweetener)	GMM 2

Draft reports, agenda and roster of subcommittee members will be available for public prior to the meeting and summary minutes will be available following the meeting. (See "What's New?" on the NTP web homepage at http://ntp-server.niehs.nih.gov)

Satellite Symposium at Society of Toxicologic Pathology Meeting

NTP is co-sponsoring a satellite symposium with EPL, Inc. entitled "An Exercise In Peer Review: The Pathology Working Group". It will be held at the annual meeting of the Society of Toxicologic Pathology on Saturday, June 14, 2003 in Savannah, Georgia.

The objective of this symposium is to provide continuing education on some basic and common lesions seen in toxicity and carcinogenicity studies and to generate lively and productive conversation about controversial and/or uncommon lesions.

This satellite symposium will present a mock pathology working group with audience participation. After cases are presented, the audience will vote on the diagnosis, and a brief discussion will follow. The audience will be equipped with voting units allowing for the instantaneous collection and display of responses. Cases will be available to registered attendees on May 15, 2003 via a link on the Society of Toxicologic Pathology web page: http://www.toxpath.org/

NTP Center for the Evaluation of Risks to Human Reproduction (CERHR)

NTP-CERHR Monograph on Phthalates

The CERHR has a new monograph series and the first is "NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of Di-*n*-Butyl Phthalate (DBP)." The monograph is available to the public and was sent to appropriate federal and state health and regulatory agencies.

This monograph includes three parts:

1) the NTP brief, which presents the NTP's interpretation of the available data and its conclusions on the potential for DBP to cause adverse developmental and reproductive effects in humans,
2) the expert panel report, and
3) all public comments on the expert panel report.

The CEHRH convened expert panels to evaluate seven phthalates. The monographs for the other six are in process and will be posted on the CERHR web site (http://cerhr.niehs.nih.gov) when completed.

Ethylene Glycol and Propylene Glycol Exposures Panel Convened

The CERHR convened an expert panel on February 11-13, 2003, in Alexandria, Virginia, to evaluate whether or not exposure to ethylene glycol or propylene glycol is a reproductive and/or developmental hazard.

Ethylene glycol was selected because

1) it is a high production volume chemical,
2) there is the potential for widespread occupational and general population exposures due to its use in heating and cooling systems (e.g., automotive antifreeze), and
3) there is published evidence from laboratory studies of developmental toxicity resulting from its exposure.

Propylene glycol is used commercially as an intermediate in the manufacture of unsaturated polyester resins and in the production of plasticizers. It was selected for evaluation because of

1) its similarity in structure to ethylene glycol and
2) the potential for widespread human exposure through its use in food, tobacco, pharmaceutical products, cosmetics, various paints and coatings and as an antifreeze and de-icing solution.

The expert panel reviewed and evaluated the available scientific evidence on ethylene glycol and propylene glycol in three primary areas: human exposure, reproductive and

developmental toxicity, and metabolism. They considered the quality, quantity and strength of the evidence in their deliberations about the potential for either chemical to cause adverse effects on human reproduction and/or development.

For ethylene glycol, the expert panel concluded that there was "negligible concern" for developmental toxicity and reproductive toxicity at current estimated levels of human exposure.

For propylene glycol, the expert panel concluded "that current estimated exposures to propylene glycol are of negligible concern for [causing] reproductive or developmental toxicity in humans."

The reports from the evaluations of ethylene glycol and propylene glycol will be posted on the CERHR website (http://cerhr.niehs.nih.gov) and made available from the CERHR in printed text. The CERHR will solicit public comment on the reports through an announcement in the Federal Register. Following this comment period, the CERHR will prepare an NTP-CERHR monograph on each chemical.

Workshop on Reproductive Effects of Thyroid Toxicants

The CERHR sponsored a workshop "Thyroid Toxicants: Assessing Reproductive Health Effects" on April 28 - 29, 2003 at the Holiday Inn Old Town Select Hotel in Alexandria, Virginia. The objectives of this workshop are two-fold:

1) To discuss the optimal design of tests to detect adverse reproductive and developmental effects resulting from chemical-induced thyroid dysfunction.
2) To discuss the relevance of thyroid-related adverse reproductive and developmental effects observed in rodents for predicting adverse effects in humans.

The agenda included plenary talks with time set aside for general discussion. Additional information is available on the CERHR web site (http:://cerhr.niehs.nih.gov).

Future Expert Panel Evaluations

The CERHR plans to conduct expert panel evaluations on the potential reproductive and/or developmental toxicity of fluoxetine hydrochloride (Prozac®; Sarafen™, and acrylamide. Dates for the two expert panel meetings are not yet set, but are tentatively planned for late 2003 and early 2004.

Fluoxetine hydrochloride (Prozac®; Sarafem), an antidepressant, was selected due to sufficient reproductive and developmental animal data, human exposure information, and public concern. Under the name Sarafem™, it is being prescribed to treat premenstrual dysphoric disorder (PMDD), potentially increasing the number of exposures to women of childbearing age. The FDA recently approved it for use in 7-17 year-olds.

Acrylamide (CAS RN 79-06-1) is used in the production of polyacrylamide, in molecular biology procedures such as electrophoresis, and in the synthesis of dyes, adhesives, contact lenses, soil conditioners, and permanent-press fabrics. It is a neurotoxicant and in animal studies has been shown to be a carcinogen, germ cell mutagen, and reproductive toxicant. Acrylamide was selected due to the recent public concern for human exposures through its presence in starchy foods treated at high temperatures, *e.g.*, french fries, potato chips. There are recent data available on occupational exposure, bioavailability, and reproductive toxicity.

Special Session at the SOT 42nd Annual Meeting and ToxExpo 2003

"Medicinal Herbals and Dietary Supplements"

Dr. Cynthia S. Smith of the Laboratory of Pharmacology and Chemistry was a co-presenter at a well-attended continuing education course on herbals and dietary supplements offered at the annual meeting of the Society of Toxicology (SOT) annual meeting in March 2003. Her topic was the characterization and use of herbal medicines and dietary supplements in bioassays. The NTP is presently conducting studies on the following medicinal herbals and herbal components: aloe vera gel, black cohash, comfrey, ginseng and ginsenosides, goldenseal, kava kava, pulegone, thujone, and extracts of grape seed, pine bark, black walnut, *Echinacea purpurea*, *Ginkgo biloba* and milk thistle.

Medicinal herbals and other dietary supplements are consumed by an estimated one-third of the U.S. population. Over 1500 botanicals are sold as dietary supplements, or ethnic traditional medicines. Their use has increased substantially since passage of the 1994 Dietary Supplement Health and Education Act. Herbal formulations are not subjected to FDA pre-market toxicity testing to assure their safety or efficacy. However, there is an increased public awareness of the need to conduct toxicity studies on herbs and herbal ingredients and many government and private laboratories are contributing to this effort.